

THE ORIGIN OF GLYCINE IN VIVO

BY

CHARLES FREDERICK KADE, JR.

B.A., Carleton College, 1936

M.S., North Dakota Agricultural College, 1938

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE SCHOOL OF
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CHAPTER I

THE ORIGIN OF GLYCINE IN VIVO

INTRODUCTION

McCoy and Rose¹ have proved conclusively that glycine is dispensable for the rat. Therefore, the amino acid must be manufactured in vivo. Knoop² has suggested that the α -amino- β -hydroxy acids are precursors of glycine. It was the purpose of this investigation to obtain experimental evidence as to the role, if any, of two of these compounds, namely, serine and threonine, in glycine synthesis.

EXPERIMENTAL

This investigation was carried out in two species of animals, the rat and the rabbit. The subjects were forced to manufacture large quantities of glycine for the detoxication of benzoic acid which was fed as the sodium salt. It has been shown by Griffith³ that the proportion of the benzoic acid excreted as hippuric acid depends upon the availability of glycine.

The rats were fed a basal diet devoid of glycine and serine and containing only the minimum level of threonine (0.5 per cent). The nitrogenous portion of the food was supplied in the form of highly purified amino acids. The ration contained 2 per cent of sodium benzoate, as this amount was found to lower substantially the rate at which the animals grew. The rats were divided into several groups. All were allowed to grow for 40 days, and the urines were collected during the last 24 days. The urines were analyzed for total benzoic acid by the method of Kingsbury and Swanson,⁴ and for hippuric acid by the method of Griffith.³ Altogether eleven litters of rats were used. The experiment was repeated three times with similar results. The third experiment was the most carefully controlled. Each diet was made equivalent in nitrogen content, and the intake of all the rats was held to the same amount. The negative controls were placed on the basal diet. On analysis of their urines 55-68 per cent of the total benzoic acid eliminated was found to have been excreted as hippuric acid. The positive controls were fed a diet to which $1\frac{1}{2}$ equivalents of glycine had been added. In this group 84-100 per cent of the excreted benzoic acid was found to be in the form of hippuric acid. Another group of animals was administered a ration supplemented by the addition of 3

equivalents of *dl*-serine. These subjects eliminated 69-89 per cent of the benzoic acid as hippuric acid. The addition of 3 equivalents of *dl*-threonine to the diet resulted in the excretion of 76-100 per cent of the benzoic acid as hippuric acid.

The procedure of Abbott and Lewis⁵ was followed when rabbits were used. Sixty-six hundredths gram of benzoic acid (as the sodium salt) per kilo of body weight was administered to the animals. In each case a 6-hour urine sample was collected and analyzed for total benzoic and hippuric acids. The data obtained show that 70-80 per cent of the benzoic acid excreted during this period was conjugated with glycine. In contrast to this if 11½ equivalents of glycine were fed with the sodium benzoate, 91-98 per cent of the benzoic acid excreted was detoxified by hippuric acid formation. The administration of serine also resulted in an increase in hippuric acid formation. Under this condition 75-100 per cent of the benzoic acid was eliminated as hippuric acid. On the other hand, when threonine was given, the results obtained were not consistent.

SUMMARY

Experiments making use of the detoxication of benzoic acid in the rat have shown that glycine, serine, and threonine increase the proportion of benzoic acid which is excreted in the form of hippuric acid. The data appear to warrant the conclusion that serine and threonine may serve as precursors of glycine in the rat. In contrast to this, in the rabbit only glycine and serine have been shown to increase consistently the proportion of benzoic acid which is eliminated in the form of hippuric acid. The data appear to justify the conclusion that serine may be one of the precursors of glycine in the rabbit. On the other hand, the findings with threonine were not sufficiently consistent to warrant interpretation.

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CHAPTER II

GROWTH ON A MIXTURE OF SYNTHETIC AMINO ACIDS

INTRODUCTION

Many attempts have been made to grow animals on a diet in which the nitrogen is furnished entirely by synthetic amino acids.¹ Of these only one experiment, and that of very short duration, has been reported² in which growth was obtained. The present investigation, conducted under more carefully controlled conditions, involved the growth of animals upon a diet containing only nine synthetic amino acids.

EXPERIMENTAL

Young albino rats were given a ration containing adequate amounts of fats, carbohydrates, minerals, and vitamins. The protein requirement was met entirely by the addition of a mixture of synthetic amino acids. Since no synthetic arginine was available, the mixture was composed of lysine, tryptophane, histidine, phenylalanine, leucine, isoleucine, threonine, methionine, and valine, each of which was added at a level considerably above the minimum.³

The rats were allowed to grow for 28 days on this diet. At the end of this time, the ration was supplemented by the addition of natural arginine. The subjects grew approximately 0.86 gm. per day during the period when no arginine was given, and about 1.63 gm. per day after arginine had been added to the food. This constitutes the most successful attempt ever reported in inducing growth upon simplified diets of this nature, and appears to warrant the assumption that natural amino acids isolated from proteins are not better sources of nitrogen than are the corresponding synthetic compounds.

SUMMARY

Growth has been obtained on a diet in which the nitrogen was furnished in the form of nine synthetic amino acids. It is believed, therefore, that synthetic amino acids are just as satisfactory for growth purposes as are the natural products.

The growth rate was found to be nearly doubled by the addition to the food of 0.2 per cent arginine. This appears to necessitate a reinvestigation of the dietary significance of arginine. Possibly this amino acid may be much more important in mammalian nutrition than has hitherto been assumed.

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VITA

The writer was born April 4, 1914, at Sheboygan, Wisconsin, where he obtained his elementary and high school education. He attended Carleton College from 1932 to 1936, and in June, 1936, received a Bachelor of Arts degree with honors in Chemistry from that institution. The academic years 1936 to 1938 were spent at North Dakota Agricultural College, where he held a teaching assistantship, and from which school he received a Master of Science degree. In the fall of 1938 he entered the Graduate School of the University of Illinois. During the first semester he held an assistantship in inorganic chemistry. Since February, 1939, he has held a special research assistantship in biochemistry.



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